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## human neutral Sphingomyelinase (NSM) Gene Sequence

1	ACCGCGGGCGTCGCTGGAGAGTCGAGCCGCTAGCGCCCTGGAGCTCCCAACCATGA	60
	TGGCGCCGGCAGCAGCTCTCAAGCTCGGCGATCGCGGGACCTCGAGGGGTTGGTACT	
	E I	
61	AGCCCAACTTCTCCCTGCGACTGCGGATCTCAACCTCAACTGCTGGTGAGTGCCTCTGC	120
	TCGGGTTGAAGAGGGACGCTGACGCCTAGAAGTTGGAGTTGACGACCACTCACCGCAGACG	
121	GGAGTGCGGTCTGGGGCCACCTTCCGTTCCGACCCATGCAGCCTCCCTCCCCCTATCCC	180
	CCTCACGCCAGACCCCCGGTGGAAAGGCAGCGTGGTACGTGGAAAGGAGGGGATAGGG	
181	GCCCCACGATCTCAGGGTGTAGGGAAACCCGAACCTCAAAGTCCACATCTGGCCCCAG	240
	CGGGGTGCTAGAGTCCCACATCCCTTTGGGCTTGGAGGTTTCAGGTGTAGACCGGGGTC	
241	CGCCGGTGGTCCCAGCAGTCGCTCCCTGGCCCTCTCCCTCTAGGGCATTCC	300
	GC GGCCACCAAGGTCGTCAGCGGAGGGGACGGGGCGAGAAGGGAAAGGAATCCCCGTAAGG	
301	GTACTTGAGCAGCACCGGGCCGACCGCATGAGGCGCCTGGGAGACTTCTGAACCAGGA	360
	CATGAACCTCGTTCGTGGCCCGGCTGGCGTACTCCGCGACCCCTCTGAAAGACTTGGTCCT	
	E II	
361	GAGCTTCGACCTGGCTTGCTGGAGGGAGGTGAGATTGTGCAGCACGGTGCAGAACCCAGG	420
	CTCGAACGCTGGACCGAAACGACCTCCACTCTAACACGTGCGCACGCCCTGGGTCC	
421	CTGGGAGGGAGGGACAGACCGTCCCCTGGGAAAGACCAAGCAGGCATCCTCACCGCTTC	480
	GACCCCTCCCTGCTGGCAGGGTGACCCCTTCTGGTCTCGTAGGAGTGGCGAAG	
481	CCTCAGGTGTGGAGTGAGCAGGACTTCCAGTACCTGAGACAGAAGCTGTCACCTACCTAC	540
	GGAGTCCACACCTCACTCGCTGAAGGTCTGACTCTGCTTCGACAGTGGATGGATG	
	E III	
541	CCAGCTGCACACCACTTCCGGAGGTGAGAACCCACTGGCCTGAAGCCTGTTGTCATCCC	600
	GGTCGACGTGTGGTAAGGCGCTCCACTCTGGGTGACCCGACTTCGGACACAGTAGGG	
601	AGGAGGCTCTGGCCCTGCCAGCCCTCCCTATCCTGCCGCACTCTCCAGTCCTCCA	660
	TCCTCCGAGAACCGGGACGGTCGGGAAGGGATAGGACGGACGTGAGAGGTCAGAGGGAGGT	
661	GCCTCCTCTCCCTCTGGATGTGAGAGAAGGGAGAAGGGTGAACCAAGAAGGTCTATGACT	720
	CGGAGGGAGGGAGACCTACACTCTTCCCTTCCACTTGGTTCTCCAGGAACTG	
721	TCAGCCCATTTCAGCTTGTGTTCTGGCTGCCCTATACTCTCCAAAGGCCGTGCCCTTG	780
	AGTCGGGTAAAGTCGAAACAAAAGACCGACGGCATATGAGGAGGTTCCGGCAGCGGAAC	
781	GTTCTAGGGCTAGTCCCAGCAGTAGAAAAAGAAAAAAATAGCTGATCAGAGCTGGAGAC	840
	CAAGATCCCAGGGTCTGTCATCTTTCTTTTTATCGACTAGTCTCGACCTCTG	
841	AAAGGGAGGGAGAAGGGCTGGGTGTCTCCCTGTTTCTGGTATTAGCAGGGCTTG	900
	TTCCCTCCCTTCTCCGACCCACAGAGAGGGACAAAAAGACCAATATTGTCCCGAAC	

Figure 1-1

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1861 CTCTCCCTCTCCCCACATCCTAGCATGAGCCAATGATTCCCTTAGGGCTCTGAGG 1920  
 GAGAGGGAGGAAGAGGGGGTAGGATCGTACTCGTTACTAAGGAAATCCCGAGACTCC  
**E VIII**

1921 AAGGCAACACAATGGTACCCAAGAACTGNTACGTCAAGCAGCAGGAGCTGAAGCCATTTC 1980  
 TTCCGTTGTGTTACCATGGGTTCTTGACNATGCCAGTCGGTCGTCCCTCGACTTCGGTAAAG

1981 CCTTGGTGTCCGATTGACTACGTGCTTACAAGGTAGGCTCCCTCAACATGCT 2040  
 GGAAACCACAGGCCCTAACTGATCCACCAATGTTCCAGTCCGAGGAGGGAGTTGTACGA

2041 TTCATATGCTGTCTCTTGTCTACTAACCTGTCTAGATCCTTGTCAAGNTAGTCTAG 2100  
 AAGTATAACGACACAGAGAAACAGATGATTGGACACATCTAGGAAACGAGTCNATCAGATC

2101 TCTTGGACCACTGATGGGTGAAAGTGGGTAGCCGGAGCTGGTCTCTGGGAAGAGGC 2160  
 AGAACCTGGTGAECTACCCACCTTCACCCATCGGCCCTGACCAAGAGAACCTTCTCCG

2161 CCTCATATATAAGCTTCTCTNTGGCCCTTACTTTCTAGGCAGTTCTGGGTTTACAT 2220  
 GGAGTATATATTCAAGAGAGANACCGGAATGAAAGGATCCGTCAAAGACCCAAAATGTA

2221 CTCCGTAAAGAGTTTGAAACCACTACAGGCTTGACCCCTNACAGGGCACCCCCCTCTC 2280  
 GAGGACATTCTCAAAACTTGGTGTGTCGAAACTGGGANTGTCCCCGTGGGGGAGAG

**E IX**

2281 TTGATCATGAAGCCCTGATGGCTACTCTGTTGTGAGGCACAGCCCCCACAGCAGAAC 2340  
 AACTAGTACTTCGGGACTACCCATGAGACAAACACTCCGTGTGGGGGGTGTCTTGG

2341 CCAGCTCTACCCACGGTGAGTCACCCCCACCCCTTCCCTGGCCCTTGCCCCGTTGAAGC 2400  
 GGTGAGATGGGTGCCACTCACTGGGGTGGGAAGGAACCGGGAACGGGGCGAACCTCG

2401 AGCCCTTCACTCTGACTCTCCCTGCCCACTGCCCTGCTCTGTTGTAGGACCAGCAG 2460  
 TCGGGAAAGGTGAGAACTGAGAGAGGACGGGTGACGGGACGAGACAACATCCTGGTCGT

2461 AGAGGTGCCGTTGATGCTGTGCTAAAGGAGGCTGGACGGAGCTGGGTCTGGGATGG 2520  
 TCTCCAGCGGCAACTACACACACGATTTCCCGGACCTGCCCTGACCCAGACCCGTACC

2521 CTCAGGCTCGCTGGTGGGCCACCTTCGCTAGCTATGTAATTGGCCTGGGCTGCTTCTCC 2580  
 GAGTCCGAGOGACCAACCCGGTGGAAAGCGATCGATAACACTAACCGGACCCGACGAAGAGG

**E X**

2581 TGGCACTGCTGTGTCCTGGCCGCTGGAGGAGGGCCGGGAAGCTGCCATACTGCTCT 2640  
 ACCGTGACGACACACAGGACCGCCGACCTCCCTCCCCGGCCCTTGACGGTATGACGAGA

2641 GGACCCCCAGTGTAGGGCTGGTGTGGCAGGTGCAATTCTACCTCTTCCACGTACAGG 2700  
 CCTGGGGGTACATCCGACCACGACACCCGTCCACGTAAGATGGAGAAGGTGCATGTCC

2701 AGGTCAATGGCTTATATAGGGCCCAAGGCTGAGCTCCAGCATGTGCTAGGAAGGGCAAGGG 2760  
 TCCAGTTACCGAATATATCCCCGGTCCGACTCGAGGTGCTACACGATCCTTCCCGTTCCC

2761 AGGCCCAAGGATCTGGGCCAGAGCCTCAGCCAGCCACTCCTGGGAGCAGGAGGGGG 2820  
 TCCGGGTCTAGACCCGGGTCTGGAGTCGGTGGGATGAGGACCCGTCGTCTCCCCC  
 ACAGAACTAAAGAACAAATAAAGCTGGCCCCAA

Figure 1-2

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2821 -----+-----+-----+--- 2852  
TGTCTTGATTTCTTGTATTTCGAACCGGGTT

Figure 1-3

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## Mouse Neutral Sphingomyelinase (nSMase) gene sequence

TNGANNCTGTTAGCTCCAGNCGGTNGGTCGCCGTNCTAGNCNNATCTNTATAGCTCTTC  
 1 -----+-----+-----+-----+-----+-----+-----+ 60  
 ANCTNNGACAATCGAGGTCNGGCCANCCAGCGGCANGATCNGNNTAGANATATCGAGAAG  
  
 GTTGCAGCNCAATTNNNTCTCAATAAANGATNCANCCCTATGACAGAACGTGGACCCC  
 61 -----+-----+-----+-----+-----+-----+-----+ 120  
 CAACGCTCGNGTTAANNAGAGTTATTCNCCTANGTNNGGATACTGTCTTGCACCTGGGG  
  
 CGCCCGCCANCNCANGNGANACCGCGGCATGGNCTGAGGTGCNCANGGTGCTGGGGCG  
 121 -----+-----+-----+-----+-----+-----+-----+ 180  
 GCGGGCGGTNGNGTNCNTTGGCGCCGTACCCNGACTCCACGNNTNCACAGACCCCGC  
  
 AGGGGTTACCTCAGCGATGGTCTTGACACCTGAAAGCTGGAGCTTTGAANAGCCCCAN  
 181 -----+-----+-----+-----+-----+-----+-----+ 240  
 TCCCCAATGGAGTCGCTACCAGAAAATGTGGACTTCGACCTCGAAAACTTNTCGGGGTN  
  
 CACCTTCAGCTTCAGGGCGGCTCNGGCGAACCGCACGTGANATGCTGGGGCTTCGA  
 241 -----+-----+-----+-----+-----+-----+-----+ 300  
 GTGGAAGTCGAAGTCCCCGCCGAGNCCGGTGGCGTGCACNTACGACCCCCGAAGCT  
  
 CTTGGGCCGGCACGGNTGCTGGTGGCATGGAANNNACAGNACAGAGCCCGNACACAA  
 301 -----+-----+-----+-----+-----+-----+-----+ 360  
 GAACCCGGCCGTGCCNACGACCCACCGTACCTNNNTGTCNTGTCGGGCCNTGTGTT  
  
 ATANTGCGAGTCGCCANGNAACCGCTGGCTCCTCCCCAACGCCCCNCAAGGGGGCGGA  
 361 -----+-----+-----+-----+-----+-----+-----+ 420  
 TATNACGCTCAGCGGTNCNTTGGCGCACCGAGGGCTTGCGGGNGTTCGGCCCT  
  
 CCTGAGTGAAGTTCNTGGCGGGGCTCNATCAACTTCAAGCCTGTTGCTGGTGGAAAGCC  
 421 -----+-----+-----+-----+-----+-----+-----+ 480  
 GGACTCACTCAAGNACCCGCCCCGGAGNGTAGTTGAAGTTCGGACAACGACCACCTTCGG  
  
 GAGCCGGGAACAGGGAGGAACCTGTAGGCCGGTGGATAACCCACCGAAGGACCTA  
 481 -----+-----+-----+-----+-----+-----+-----+ 540  
 CTCGGCCCTTGTCCCTCCTGGACATCCGGCGCCACGCCATTGGTGGCTCCTGGAT  
  
 AGAATCTGGAACAGTCCACCCGAGATTCCCTCCAGGACTGCCGGGACTCTCGCATTCA  
 541 -----+-----+-----+-----+-----+-----+-----+ 600  
 TCTTAGACCTTGTCAAGGTGGCTCTAAGGAAGGTCTGACGGCCCTGAGAGCGTAAGT  
  
 GCGCCGGATTTGCAAGCCGACCTTCTTCCGGTGGATGACGGCTTGTCCAGTAACG  
 601 -----+-----+-----+-----+-----+-----+-----+ 660  
 CGGGCCCTAACGTCGGCTGGAGAAAGGCCACCTTACTGCCGAAACAGGGTCATTGC  
  
 CAGGAGTCNNCCCCACCCCCAACAGCTCGCTTCTGGTGGCAGCGCAGGATAGG  
 661 -----+-----+-----+-----+-----+-----+-----+ 720  
 GTCCTCAGNNNGGGTGGGGTGGTCGAGCGAAGGACCCAGCCCCGTCGCTATCC  
 Start  
 GCAATAAGCCTGTGCGCGCAATCCGCTCGCCCTTGTCCGAAGCACTCCAGCCATG  
 721 -----+-----+-----+-----+-----+-----+-----+ 780  
 CGTTATTGGACACGCGCGTTAGGCGGAGCGGGGGAACGAGGCTCGTGAGGTGGTAC  
  
 AAGCTCAACTTTCTCTACGGCTGAGAGTTCAATCTCAACTGCTGgtaaagtgt  
 781 -----+-----+-----+-----+-----+-----+-----+ 840  
 TTGAGTTGAAAAGAGATGCCGACTCTCAAAAGTTAGTTGACCGACcattcattcacga

Figure 2-1

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cccaggcggtgggCTGCAGCCTCGGAGCCACCTCCAGTCCCCTCTGCACATGCCAGGA  
 841 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 900  
 ggggtccgcacccGACGTCGGAGCCTCGGTGGAAGGTCAAGGGAGAGCGTGTACGGATCCT  
  
 AGGAAGCAGGTCTTCAGCCGAGCTAGACCCCTGTCCCTCCGAACCACCAAAGTCCAC  
 901 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 960  
 TCCTTCGTCAGAAGAAGTCGGCTCGATCTGGGACAGGAAGGGCTGGTGGTTCAAGGTG  
  
 ATCGCCTAAAGACCAAGAGCTGGGTGGTGCAGCAATCACCAAAGTCCCTATCATCCAAA  
 961 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1020  
 TAGCGGATTCCTGGTCTGAACCCACCAACGTCGTTAGTGGTTCAAGGATAGTAGGTT  
  
 GCTGAGGTGATGACAGCAGTAATCGTCCAAACCTGGCCATGTCTTCCTTTAAATGA  
 1021 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1080  
 CGACTCCACTACTGTCGTCAATTAGCAGGGTTGGACGGGCTACACAAAGCAAAATTACT  
  
 TTTACTTTATTTATGTACATTGGTGTGCTGTATGTATGTCTGTGTGAAGGTGC  
 1081 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1140  
 AAAATGAAAATAAAATACATGTAACCACAAAACGGACATACATACAGACACACTCCACG  
  
 CAGATTCTCTGGAACTGGAGTTACAGACAGTTGTAAGCTGTCATGTGCTTGCTGGAAATT  
 1141 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1200  
 GTCTAAGAGACCTTGACCTCAATGTCGTCAACATTGACAGTACACGAACGACCTTAA  
  
 GAACTGCTGACCCATCTCTGCCCCCTGCGTCCTCCACCCCTTTAGGGACATCCCCT  
 1201 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1260  
 CTTGACGACTGGTAGAGAAGACGGGGGACGCAGGAGGTGGGGAAAATCCCTGTAGGGGA  
  
 ACCTGAGCAAACATAGGGCGGACCGCATGAAGCGCTGGGAGACTTCTGAACCTGGAAA  
 1261 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1320  
 TGGACTCGTTGTATCCCGCTGGCGTACTCGCAACCCCTCTGAAGACACTGAACCTTT  
  
**E II**  
 ACTTTGATCTGGCTCTCTGGAGGAGGTGAGGTTGTAGGGCAGGCTAGGTTGGAGGGAGGG  
 1321 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1380  
 TGAAAATAGACCGAGAGGACCTCCACTCCAAACATCCCGTCGATCCAACCTCCCTCCC  
  
 CAGCAGGCGGCAGCGGGCGCAGGAAAACCTGTTCTGCTTGGGATGAAATCCCAAGCAA  
 1381 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1440  
 GTCGTCCGCCGTCCGCCCGTCTTTGAACAAGACAGAACCCCTACTTAGGGTTCGTT  
  
 GTATCCTCACCTCTTCCCTCCAGGTGTGGAGTGAGCAGGACTTCCCAGTACCTAAGGCAA  
 1441 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1500  
 CATAGGAGTGGAAAGAAGGAGGTCCACACCTCACTCGTCTGAAGGGCATGGATCCCGTT  
  
**E III**  
 AGGCTATCGCTACCTATCCAGATGCACACTACTTCAGAAGGTGAAAGCCTGTGTTCTC  
 1501 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1560  
 TCCGATAGCGAGTGGATAGGTCTACGTGTGATGAAGTCTTCACTTTCCGACACAAGAG  
  
 AGCCTGTTCTCAGACGAGGAAGCTCCAACATTCTGCTTGACCCCTCGATCTCTTCC  
 1561 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1620  
 TCGGACAAGAGTCTGCTCTTCGAGAGGTGTAAGAACGAACGTGGGAGCTAGAAGAAGG  
  
 TCTGGGTGTGAGAAGACGAGGCCGTACCCCTCATCTGCAAGGGCTGCTGTCTTAGGCTT  
 1621 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1680  
 AGACCCACACTCTCGTCCGGCAGTGGGAGTAGAACGTTCCGACGACAGAACCGAA  
  
 TGTTCTGGGTTGATCTTAGCAGTAGAGCTGGGAGACCGCGGAGGGGAAGAGGGCTGGCT  
 1681 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 1740  
 ACAAGACCCAACTAGAACGTCATCTCGACCCCTCTGGCGCTCCCCCTCTCCCGACCGA

Figure 2-2

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GGGTACTCCCCCTTGCTTCTGGTTATTAAGCAAGAGTTGGTTTCAGCGGGATGAT  
 1741 -----+-----+-----+-----+-----+-----+-----+ 1800  
 CCCATGAGGGAGGAACGAGAAGACCAATAATCGTTCTAACCAAAAGTCGCCCTACTA

**E IV**  
 AGGCAGTGGCCTCTGTGTGTTCTCAAACACCCAATCCAGGAATCTTCCAGCATGTCTA  
 1801 -----+-----+-----+-----+-----+-----+-----+ 1860  
 TCCGTACCGGAGACACACAAGAGGTTGTGGGTTAGGTCTTAGAAGGTCGTACAGAT

CAGTCTGAATGGTTACCCCTACATGGTAAGGATCTTCCCTATCCTTGCTAACACAGAC  
 1861 -----+-----+-----+-----+-----+-----+-----+ 1920  
 GTCAGACTTACCAATGGGGATGTACCATTCCTAGAGAAGGGATAGGAACGATTGTGTCG

TGGACGCAGCCTTCTGGGGCCTTGGCAGGAGGGTGTCACTACCCCTGAGTTTTGTCTTC  
 1921 -----+-----+-----+-----+-----+-----+-----+ 1980  
 ACCTGGCTCGGAAGGACCCCGAACCGTCTCCCACAGTCATGGGACTCAAAAACAGAAG

TCTTGCTGCAGTCCATCATGGAGACTGGTTCTGTGGGAAGTCTGTGGGCTGCTGGTG  
 1981 -----+-----+-----+-----+-----+-----+-----+ 2040  
 AGAACGGACGTCAAGGTAGTACCTCTGACCAAGACACCCCTTCAGACACCCCCGACGACCAAC

**E V**  
 CTCCGTCTAAGTGGACTGGTGCTCAATGCCAACGTGACTCATGTGAGTGGGCTAGCCAG  
 2041 -----+-----+-----+-----+-----+-----+-----+ 2100  
 GAGGCAGATTACCTGACCAACGAGTTACGGATGCACTGAGTACACTCACCCGATCGGTC

GCTTAGGCAGTGGGCAAGCAGCCCAATGCTATGGTGGAGAAGAGACGCCACTAGTTAGT  
 2101 -----+-----+-----+-----+-----+-----+-----+ 2160  
 CGAATCCGTACCCAGTTCGTGGGTTACGATACCAACCTCTCTGCGGTGATCAATCA

TCTGCTGCCTGGGATAAGGCATGGGATCAGAAGCTAGCATTGGCAAGGTTCACCCATT  
 2161 -----+-----+-----+-----+-----+-----+-----+ 2220  
 AGACGACGGACCCCTATTCCGTACCCCTAGTCTCGATCGTAACCGTTCCAAGTGGTAA

CCCTGTCACACTCTGCCATGTGACAGATGACAAGCTTGATTCAAGACAGCCTCTCTTGA  
 2221 -----+-----+-----+-----+-----+-----+-----+ 2280  
 GGGACAGTGTGAGACGGTACACTGTCTACTGTTCGAACTAAGTCTGTGGAAAGAGAAACT

TTTCACCTATTCCACTTTAGCTACATGCTGAGTACAGCCGACAGAAGGACATCTACTTIG  
 2281 -----+-----+-----+-----+-----+-----+-----+ 2340  
 AAAGTGGATAAGGTGAAATCGATGTACGACTCATGTCGGCTGCTTCTGTAGATGAAAC

**E VI**  
 CACACCGTGTGCCAACGTTGGAACTGGCCAGTTCAATCCAGTGTGAGCCTGGGCT  
 2341 -----+-----+-----+-----+-----+-----+-----+ 2400  
 GTGTGGCACACCGGGTTCGAACCCCTGACCGGGTCAAGTAGGTACACACTCGGACCCGA

TGATGGGGCTGTGGGTGGGACGGGGTTGAGGGATGNGNAANTTATCCTTGAAAGAGGG  
 2401 -----+-----+-----+-----+-----+-----+-----+ 2460  
 ACTACCCCCGACACCCCAACCCCTGCCCAACTCCCTACNCNTNAATAGGAACCTCTCCC

CACATAATAAGGAAAGAATTCCCTCTGCCCTCTTCCCCAACACTCAGCCACACATCCA  
 2461 -----+-----+-----+-----+-----+-----+-----+ 2520  
 GTGTATTATTCCCTTAAAGGAGGAACGGCGAGAAGGGGGTTGAGTCGGTGTAGGT

**E VII**  
 AGAATGCAGATGTGGTTCTATTGTGTGGAGACCTCAATATGCACCCCAAAGACCTGGGCT  
 2521 -----+-----+-----+-----+-----+-----+-----+ 2580  
 TCTTACGTCTACACCAAGATAAACACACCTCTGGAGTTACGTGGGTTCTGGACCCGA

Figure 2-3

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GCTGCCTGCTGAAAGAGTGGACAGGGCTCCATGATGCTTCGTTGAGACTGAGGACTTTA  
 2581 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2640  
 CGACGGACGACTTTCTCACCTGTCCCGAGGTACTACGAAGCAACTCTGACTCCTGAAT  
  
 AGGTGAGAGACTGTTCCCACCAACTCCACACTTGTCCAGTCTTCCTGTCTTAGCAT  
 2641 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2700  
 TCCACTCTGACAAAGGGTGGTTGAGGTGTGAACAAGGTAGAAGGACAGAGAATCGTA  
  
 CCTAGCCACCTGTTCCCTAGGGCTCTGATGATGGCTGTACCATGGTACCCAAGAACTGC  
 2701 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2760  
 GGATCGGTGGACAAAGGGATCCCGAGACTACTACCGACATGGTACCATGGTTCTTGACG  
  
**E VIII**  
 TACGTCAGCCAGCAGGACCTGGGACCGTTCCGTCTGGTATCCGGATTGATTACGTGCTT  
 2761 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2820  
 ATGCAGTCGGTCGTCCCTGGACCCCTGGCAAAGGCAGACCATAGGCCTAACTAATGCACGAA  
  
 TACAAGGTCAAGGCTCTTATTCCCGGTGTGCCTTCTCCAGTATCTTCCTTCCTGTCACT  
 2821 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2880  
 ATGTTCCAGTCCGAGAATAAGGGCCACACCGAAGAGGTATAGAAGGAAGGGAGACAGTGA  
  
 AGCCCACGCTTTAGTCAGCTACAGTCTGGGCCACTGATGGCTAAAGAATAGAACCTG  
 2881 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 2940  
 TCGGGTGCAGAAATCAAGTCGATGTCAGAACCCGGTACTACCGATTCTTATCTTAGGAC  
  
 TCGGCTGGTTCTCTGGGAGAATTAAAGCTTCTCCATGTTCTGCTCTCCTAGGCAGTCT  
 2941 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3000  
 AGCCGACCAAGAGACCCCTCTAAATTGAGAGGTACAAGAACGAGAACGGATCCGTCAGA  
  
 CTGAGTTCCACGTCTGCTGTGAGACTCTGAAAACACTACAGGCTGTGACCCCTCACAGTG  
 3001 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3060  
 GACTCAAGGTGCAGACGACACTCTGAGACTTTGGTATGTCCGACACTGGGAGTGTCAAC  
  
**E IX**  
 ACAAGCCCTCTCTGATCACGAGGCCCTCATGGCTACTTGTATGTGAAGCACAGCCCC  
 3061 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3120  
 TGTTCGGGAAAGAGACTAGTGCTCCGGAGTACCGATGAAACATACACTTCGTGTCGGGG  
  
 CTCAGGAAGACCCCTGTAUTGCTGTGGTAAGCAGCATTTCCTTGCCCCCTACTTTA  
 3121 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3180  
 GAGTCCTTCTGGGACATGACGGACACCATTGCTGTAAAGGAAACGGGGAGATGAAAT  
  
 AGGCAGCCCCGCCCTCCATCCTGACCCCTCCCTGCTCTACGTTCTCTCTTTCCAGGCC  
 3181 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3240  
 TCCGTCGGGCGGGAGGTAGGACTGGGAGGGGACGAGATGCAAGAGAGAAAAAGGTCCGG  
  
 ACTGGAAAGGTCCGATTGATCAGCGTGCTAAGGGAGGCCAGGACAGAGCTGGGCTAGG  
 3241 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3300  
 TGACCTTCCAGGCTAAACTAGTCGCACGATTCCCTCCGGTCTGCTCGACCCGATCC  
  
**E X**  
 CATAGCTAAAGCTCGCTGGTGGGCTGCATTCTCTGGCTATGTGATCGTTGGGGCTGTC  
 3301 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3360  
 GTATCGATTCGAGCGACCACCCGACGTAAGAGACCGATACTAGCAAACCCCCGACAG  
  
 CCTTCTGGTGTGCTGTGTCCTGGCTGCAGGAGAAGAGGCCAGGGAAAGTGGCCATCAT  
 3361 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 3420  
 GGAAGACCACAAACGACACACAGGACCGACGTCTTCTCCGGTCCCTCACCGGTAGTA

Figure 2-4

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CCTCTGCATACCCAGTGTGGGTCTGGTCTGGTAGCAGGTGCAGTCTACCTCTTCCACAA  
 3421 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3480  
 GGAGACGTATGGGTCAACCCCAGACCCAGACCATCGTCCACGTCAAGATGGAGAAGGTGTT  
  
 GCAGGAGGCCAAGGGTTATGTCGGGCCAGGCTGAGATGCTGCACGTTCTGACAAGGGA  
 3481 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3540  
 CGTCTCCGGTCCCGAATACAGCCCCGGTCCGACTCTACGACGTGCAAGACTGTTCCCT  
  
 AACGGAGACCCAGGACCGAGGCTCAGAGCCTCACCTAGCCTACTGCTTGCAGCAGGAGGG  
 3541 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3600  
 TTGCCTCTGGGTCTGGCTCGAGTCTCGGAGTGGATCGGATGACGAACGTGGTCCCTCCC  
 stop  
 GGACAGAGCTTAAGAGCTTAACAATAAAACTTGCTTGACACACTCTAGTGGCTTACCTT  
 3601 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3660  
 CCTGTCTCGAATTCTCGAATTGTTATTTGAACGAACGTGTGAGATCACCGAGATGGAA  
  
 GTTCTTGCAAGGGCATGATGGAACTGAAGGTCACTGGCCTTGTCACTGTGTGGCTTTA  
 3661 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3720  
 CAAGGAACGTCTCCGTACTACCCCTGACTTCCAGTCACCGAACAGTGACACACCGAAAT  
  
 GAGCGTTGGCCTCTCACTTGCCTTTTGACACTCCGTCTGCCAGCACAGAGCAT  
 3721 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3780  
 CTCGCAACCGGAGAGTGAACGGAAAAACGTGTGAGGGCAGAGGACGGTGTCTCGTA  
  
 AAACCCCTGTTCATGGTCATAATCCTTTATTGTAACAAACGAAGCCTCTGACTAACAGT  
 3781 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3840  
 TTTGGGACAAGTACCACTATTAGGAAATAACATTGTTGCTCGAGACTGATTGTCA  
  
 CCAGATGGCGGGAGGTACAGCCCTGTGATGGTGTCTGCTTACGGGGCAGGGAGGCAGCT  
 3841 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3900  
 GGTCTACCGCCTCCATGTGGAAACACTACCACAGAACGAATGCCCGTCCCTCGTCA  
  
 AACCATCATCTCTAGCCCTGGGCTCCCATCTATGCAGGCATCTCTGAGCCTCCGTT  
 3901 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 3960  
 TTGGTAGTAAAGATCGGGACCCGAGGGTAGATACTGTCGGTAGAGAGACTCGGAGGAAG  
  
 CTCCCTGGAATTGNTCAGAGCAATCCGCTTGGTCACCAACCTCAAACAGCTTCTTA  
 3961 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 4020  
 GAGGACCTTAACCNAGTCTCGTTAGGGCAACCAAGTGGTTGGAGGTTTGTCAAGGAAT  
  
 AGGACCTGGTTCTCAAAANGNAAGGTNCGGGCTCCGGCTTCAATANGTTTCTTAA  
 4021 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 4080  
 TCCTGGACCAAAGAGTTTNCNTCCANGCCGGAGGCCAGAAGTTATNCAAAAGGATT  
  
 AAAGGGANGAATGAAAANCCTTAAGNNCCAACAAGGGAACCCCTGGNCCAAAAGGGGA  
 4081 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 4140  
 TTCCCTNCTTACTTTNGGAATTCTNNNGGTTGTTCCCTGGAACCCNGGTTTCCCT  
  
 CCTGGGTGGTTCCCTGGGCCAANNTTATCCAAAGGGTCAAATTGAAGGGTTAAC  
 4141 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 4200  
 GGACCCACCAAGGGNAACCCGGTTNAATAGGGTTCCCCAGGTTAACCTCCAAATTG  
  
 CCCCCAAAAANACCGNTTCCCCCGGAATTCCAAGGTTNCCCCCCCCGGCAAANC  
 4201 -----+-----+-----+-----+-----+-----+-----+-----+-----+-----+ 4260  
 GGGGTTTTNNNTGGNAAAGGGGGCTTAAAGGTTCAAANGGGGGCCGTTTNG

Figure 2-5

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TCCCTTGGGNNCCNAANCCNTGGCCCGNCTGGCTTTCCCCCTTCCCAAGNATTTC  
4261 -----+-----+-----+-----+-----+-----+-----+ 4320  
AGGAACCCCNNGGNTTNGNACCGGGCNGAACGAAAAGGGGAAAGGGTTCNATAAG

AAANNTTCCCTNGAAANCCCTTGNNTGGNAAAACNAATNANGAACCAANNN  
4321 -----+-----+-----+-----+-----+-----+-----+ 4380  
TTTNAAGGGANCCTTNGGGAACNAACCNTTGGNTTANTNCTTGGTNCGGTTNNNA

TGCCAANAAACCNTTGGCAAAGGGGNAATTCAACCAANGGGNAATTGGGAAACCC  
4381 -----+-----+-----+-----+-----+-----+-----+ 4440  
ACGGTTNTTGGNAAACCGTTCCCCNTTAAGTNGTTNCCCNTTAACCCCTTGGG

NTGGGTTTNCCTAAAGGGCCCNAANANT  
4441 -----+-----+-----+-----+-----+-----+ 4468  
NACCAAANGGGTTCCGGGNTNTNA

Figure 2-6

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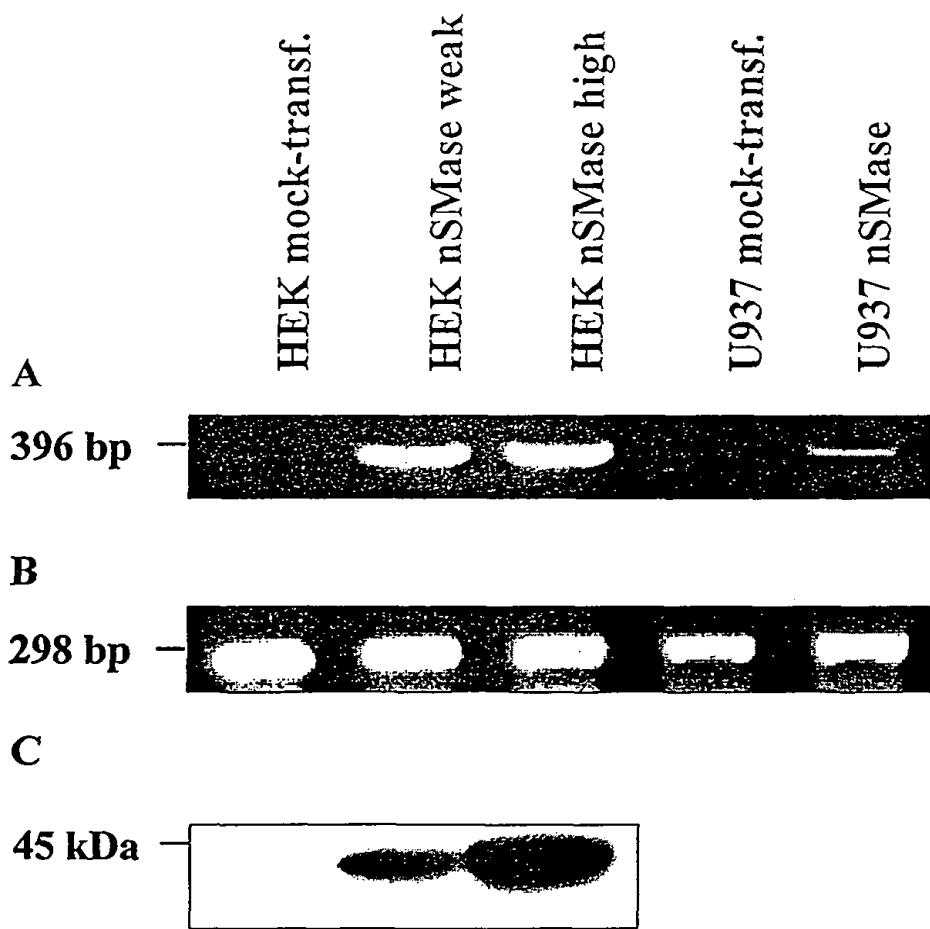


Figure 3

## mnS-Mase "konventional" Knock Out

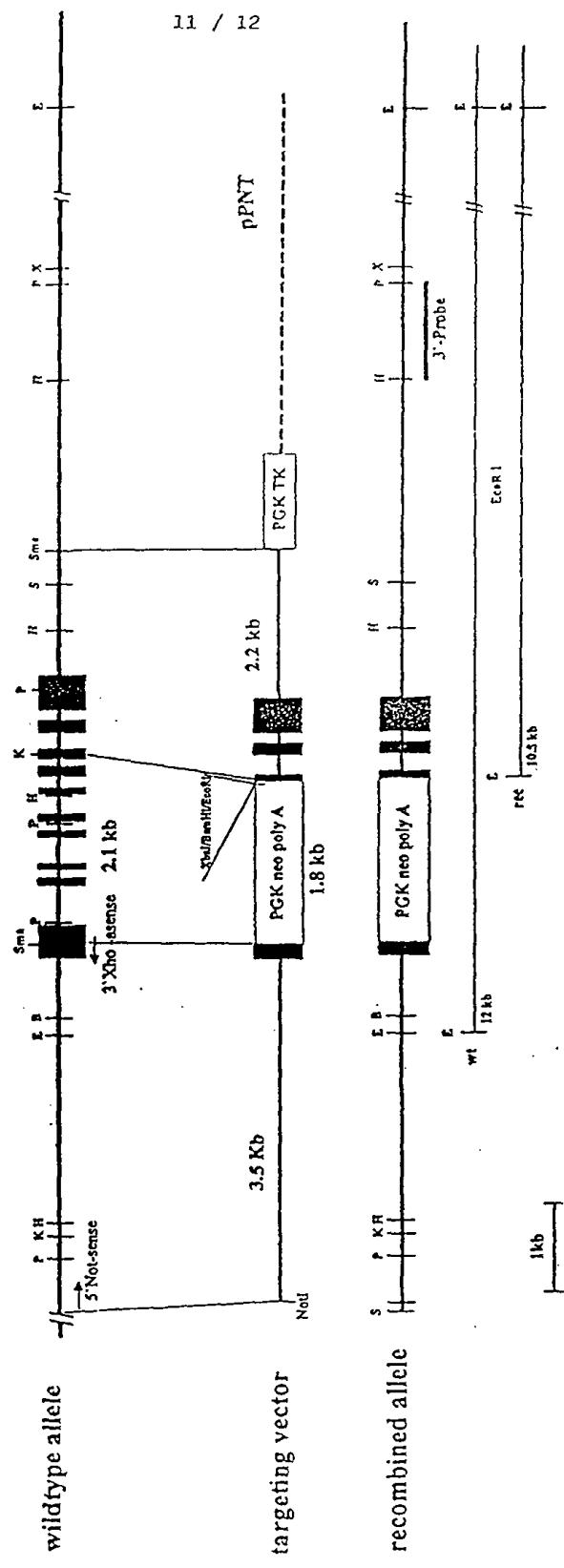


Figure 4

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## Constructs for generating transgenic mouse mutants

ubiquitin promoter	nSMase	IRES	lacZ	polyA			
polyA	rtTA	CMV	CMV-1	nSMase	IRES	GFP	polyA

Ubiquitin promoter: regulatory sequence of the ubiquitin gene, controlling a ubiquitous transcription.

nSMase: neutral sphingomyelinase

lacZ: lacZ, gene coding for  $\beta$ -galactosidase

polyA: recognition signal for the termination of transcription and polyadenylation

CMV: cytomegalovirus promoter of the cytomegalovirus gene, controlling a ubiquitous transcription.

rtTA: reverse transactivator, binds to the minimal promoter and thus controls transcription. The binding properties of the transactivator are influenced by tetracycline. The addition of tetracycline makes the transactivator bind to the minimal promoter and starts transcription, removal of tetracycline prevents the binding of the transactivator to the minimal promoter and prevents transcription.

CMV-1: minimal promoter, binding of transactivator starts transcription.

IRES: *internal ribosomal entry sequence*, viral initiation signal for translation.

Figure 5